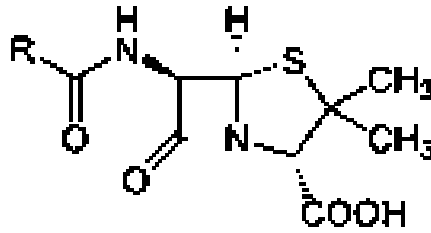


Penicillin



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Introduction

- * **antibiotics**
- * derived from **penicillin fungi**.
- * Definition of antibiotics: **killing** or **stopping** the growth of a disease-causing bacteria.



How penicillin works

- * **preventing** some bacteria from **forming new cell walls**.
- * Bacteria **cannot** complete the **process of division**
- * **Cannot** produce two new 'daughter' bacteria from a single 'parent' bacterium.
- * **resist bacterial infections**.

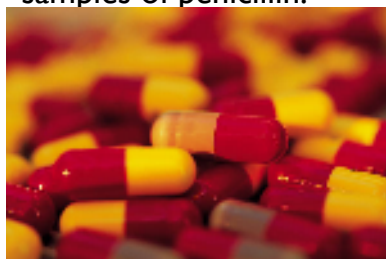


Lead Compound Discovery

- * **Alexander Fleming** contributed to the discovery of penicillin
- * Discovery process:
 - ① arranging a pile of Petri dishes where he had been growing bacteria
 - ② **not uncommon:** some mold was growing on one of the dishes
 - ③ **very unusual:** the bacteria around the mold had been **killed**.

Lead Compound Discovery

- * **Conclusion:**
- * The mold was releasing a substance that could **inhibit** the **growth** of **bacteria**.
- * Notwithstanding, he was **never able** to **purify** his samples of penicillin.

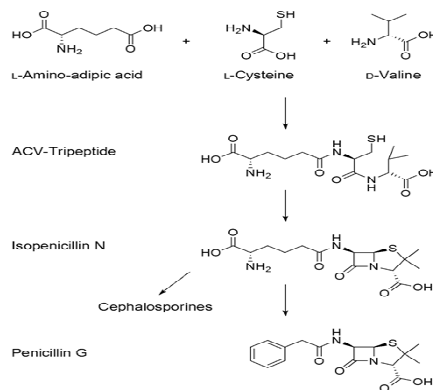


Molecular modification

Two different categories of penicillin.

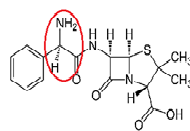
* Biosynthetic penicillin

1. natural penicillin
2. harvested from the mold itself by fermentation.

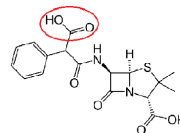


Molecular modification

- * The other form of penicillin is called **semi-synthetic**.
- * Semi-synthetic compounds:
 - **basic structure of penicillin**
 - **modified chemically by adding acyl groups that produce new properties.**



Ampicillin

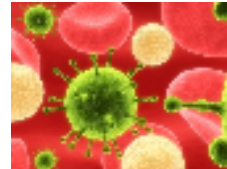


Carbenicillin

Molecular modification

Advantages:

- * **resist the acid in the stomach** so as to take the drugs orally.
- * The modification also increases the degree of **resistance to penicillinase**.
- * It has an extended range of **activity against some Gram-negative bacteria**.



Formulation development

- * developed into **different types of derivatives**
- * **Cause:** the **narrow range** of **treatable diseases**
- * Derivatives: treating a **wider range of infections**.
- * **Benzylopenicillin**, **procaine benzylopenicillin**, **benzathine benzylopenicillin** and **phenoxymethylpenicillin** are the four main types of drugs used nowadays.

Formulation development

- * **Benzympenicillin:**
- * **injection** into a vein or muscle, or via a drip into a vein.
- * **treat infections** of the lungs and airways, mouth and throat, skin or soft tissue, or ears, as well as other more rare infections.



Formulation development

- * **Procaine benzylpenicillin:**
- * **Injection**
- * a sustained release drug that is **slowly hydrolysed** to **benzylpenicillin** after deep **intramuscular injection**.
- * Its **microbiological properties** are the **same** as those of **benzylpenicillin**.



Formulation development

- * Benzathine benzylpenicillin
- * **Injection**
- * slowly **absorbed** into the circulation, after **intramuscular injection**, and hydrolysed to benzylpenicillin.
- * **drug-of-choice** when prolonged low concentrations of benzylpenicillin are required and appropriate
- * allowing prolonged antibiotic action over **2–4 weeks** after **a single IM dose**.

Formulation development

- * Phenoxymethylpenicillin:
- * has a **similar spectrum** of action to benzylpenicillin
- * **less active**
- * **not** used for **serious** infections
- * taken by **mouth** and is **more resistant** to the action of **gastric acids**



Safety Test and Human Trials

- * Safety Test on animals:
 - inject penicillin in rabbits and mice
 - cured rabbits and mice can resist bacterial infections.
 - The test on animals is successful

Safety Test and Human Trials

- * Human research trials:
 - began around 1940-1941
 - Penicillin was tried on a policeman
 - This was one of the first tests of penicillin. It had taken four days for him to improve.

Approval for marketing

- * A new drug application must include:
 - the **drug's test results**
 - **manufacturing information** to demonstrate the company can properly manufacture the drug
 - the company's **proposed label** for the drug

Manufacturing process

- * It was difficult to produce enough penicillin.
- * There were three methods to mass-produce penicillin:
 - ① **Creating the right environment**
 - ② **corn steep liquor**
 - ③ **A moldy cantaloupe**



The End